

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-9 and 11-21 are pending in the application, with claims 1 and 16 being the independent claims. Claim 10 is sought to be cancelled without prejudice to or disclaimer of the subject matter therein. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Claim Objections

The Examiner has objected to claim 10 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of the previous claim. The Examiner's objection to claim 10 is moot in view of the cancelled claim 10.

The Examiner has objected to claims 13-14 and 20 as being dependent upon a rejected base claim. The Examiner's objection will be moot upon allowance of said rejected base claims after reconsideration of the rejections in view of the provided arguments.

The Examiner has objected to claim 16, should claim 15 be found allowable, as being a substantial duplicate thereof. Applicant respectfully disagrees. Claim 15 is drawn to multiple cross-linked HA obtainable by a process according to claim 1. In contrast, Claim 16 is drawn to HA cross-linked to a further molecule of HA, with the cross-linked HA having at least two different types of bonds. Claim 15 is a product-by-

process claim having limitations relating to the processes as set forth by the claimed invention, whereas claim 16 is not limited to only these processes.

Rejections under 35 U.S.C. § 112

Claims 1-12, 15-19 and 21 were rejected under 35 U.S.C. §112, first paragraph. The Examiner has alleged that the specification, while being enabling for double cross-linked HA, does not reasonably provide enablement for multiple cross-linked HA wherein more than two chemically distinct cross-links between HA molecules are present. The Examiner has stated that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims without undue experimentation, as evaluated by weighing the considerations set forth in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Applicant respectfully disagrees and traverses this rejection.

In assessing whether any necessary experimentation is undue, *Wands* set forth several factors to be weighed in making this determination. These factors include but are not limited to the following: The breadth of the claims; the nature of the invention; the state of the prior art; the level of ordinary skill in the art; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make and/or use the invention based on the content of the disclosure.

Referring to these factors, the Examiner appears to have made a conclusory argument with minimal elaboration concerning why the claim is not enabled. The

Examiner acknowledges that cross-linked HA is known in the art, providing two exemplary documents (U.S. Patent Nos. 4,582,865 and 4,957,744). Applicant has also provided and discussed several exemplary documents in the pending specification (see for example U.S. Patent Nos. 4,582,865; 5,550,187; 5,578,661; 5,644,049; 5,800,541; Tomihata *et al.*, J.Biomed.Mater.Res., 37, 243-251, 1997, and International Patent Application WO 97/04012) . Further, the Examiner has acknowledged that the level of ordinary skill in the art is high, stating that one with ordinary skill in the art would be an organic or polymer chemist having a M.S. degree or higher. The crux of the Examiner's rejection seems to be the lack of working examples that would demonstrate the preparation of cross-linked HA wherein more than two chemically distinct cross-links between HA molecules are present.

"Compliance with the enablement requirement of 35 U.S.C. §112, first paragraph, does not turn on whether an example is disclosed." MPEP §2164.02, first paragraph. Furthermore, there is no "magical relation between the number of representative examples and the breadth of the claims; the number and variety of examples are irrelevant if the disclosure is 'enabling' and sets forth the 'best mode contemplated.'" In re Borkowski, 164 U.S.P.Q. 642, 646 (C.C.P.A. 1970). Moreover, a specification need not contain a single working example. *Id* at 645.

Against the foregoing legal standard, Applicant's specification is fully enabling. Although lack of working examples is *one* factor to be considered, particularly in unpredictable arts, it is only part of the calculus of determining whether the enablement requirement has been satisfied. In the instant application, as the Examiner has noted, Applicant has provided several working examples demonstrating the production of

double cross-linked HA. These examples demonstrate that the concept of multiple cross-linked HA, with more than one type of cross-linking bond being present, is a viable one. In no way, however, should they be construed to limit the scope of the present invention to that of only double cross-linked HA. The examples illustrate that the concept of more than one chemically distinct cross-links between HA is achievable. Progressing to the next step of more than two cross-links would have been well within the skill in the art at the time of filing by following the guidance set forth in the specification.

Moreover, Applicant has provided a sufficient amount of guidance in the specification for one skilled in the art to make not only double cross-linked HA, but multiple cross-linked HA. One issue that is examined with regard to enablement, is whether the materials required to make a compound or to practice a chemical process are disclosed in the specification. *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981). Applicant has provided, on page 6, lines 3-26 of the specification, several different types of linkages, and the preferred cross-linking agent to be used to obtain these linkages. Further, the specification, beginning on page 6, line 28 and continuing to page 9, line 5, provides enough guidance to one skilled in the chemical arts to produce multiple cross-linked HA. As discussed *supra*, the necessary chemicals required for each type of cross-linking reaction have been provided by Applicant. Determining the specific order of the multiple reactions and the precise conditions was well within the skill of the art, and would have required only routine experimentation that would not have been undue for one skilled in the chemical arts at the time of filing, contrary to the Examiner's allegation.

Furthermore, Applicant maintains that experimentation is permitted as long as the experimentation is not undue. The fact that the subject technology is complex, or that some experimentation is required is not dispositive of the enablement issue. Moreover, the burden of showing that the disclosure entails undue experimentation rests on the USPTO. In re Angstadt, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 219 (CCPA 1976).

In assessing whether the experimentation is undue, further factors to look at are quantity of experimentation, time and expense, guidance, and difficulty of the experiments. MPEP §2164.06. Applicant has provided the necessary guidance to proceed with the production of multiple cross-linked HA, as discussed *supra*. The optimization of the different reaction conditions and reaction sequences, though more time consuming than merely following an established protocol, would have been routine practice for one skilled in the chemical arts at the time of filing. Applicant has provided numerous working examples that provide guidance for the production of double cross-linked HA. Adding additional cross-linking steps to attempt to produce multiple (i.e. more than two) cross-linked HA would have imposed a minimal time and expense burden on the practitioner, and performing the assays necessary to verify the presence of multiple cross-linked HA would have been the same as the tests disclosed to assess the double cross-linked HA produced. In setting forth a conclusory argument with minimal elaboration, the Examiner has failed to demonstrate that undue experimentation is required by the disclosure. Thus, Applicant maintains that no undue experimentation would have been necessary to practice the full scope of the invention at the time of filing.

Lastly, the predictability of the art at issue is a factor to be addressed in assessing enablement. The chemical arts are often considered to be unpredictable arts due to the

very nature of the reactions involved. Applicant does not dispute this, and in fact the principle of providing more than one chemically distinct cross-links between HA molecules was unproven prior to the present invention. However, in demonstrating in the present invention that the reactions produce more than one chemically distinct cross-link between HA molecules, at the time of filing it would have been reasonably predictable to apply these same reactions to the production of multiple (*i.e.* more than two) cross-links between HA molecules. Accordingly, when all of the relevant factors set forth in *Wands* factors are weighed, particularly noting the high level of skill in the art, the sufficient guidance provided in the specification, and that the experimentation entailed is not undue, Applicant maintains that the rejection under 35 U.S.C. §112, first paragraph be reconsidered and withdrawn.

Claim 21 was rejected under 35 U.S.C. §112, first paragraph. The Examiner has alleged that the specification, while being enabling for cross-linked HA in the form of a film or gel, does not reasonably provide enablement for all products comprising said cross-linked HA without undue experimentation. Applicant respectfully traverses this rejection.

The Examiner acknowledges that Applicant has enabled at least two embodiments of the claimed invention (page 5, point 7 on the 11/25/02 Office Action). Moreover, Applicant has provided numerous examples of products that would utilize the cross-linked HA of the invention (see, for example, pages 15 and 16 of the specification). There is no requirement to exemplify all embodiments. If the Examiner is aware of such a requirement, he is respectfully requested to provide a citation to such. In the absence of further support for the Examiner's argument, the invention of claim 21 is enabled.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

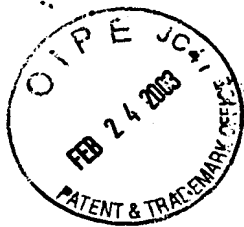
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Xiaobin ZHAO
Appl. No. 09/920,286

Version with markings to show changes made

Please cancel claim 10.

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